

Application No. 10/516,418
Amendment and Response dated September 26, 2007

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Docket No.: 60009US(49991)

REMARKS

Claims 1-45, 62-65, 95-101, 106-113 and 117 are pending in the application. Applicants have cancelled claims 2 and 12 without prejudice or disclaimer and have amended claims 1, 3, 4, 6, 13, 17, 18, 20-22, 28, 29, and 33. Claims 10, 31, 32, 34-45, 62-65, 95-101, 106-113, and 117 have been withdrawn. Claim 123 is new. Support for the addition of claim 123 can be found at least at page 21, lines 3-6, of the application as filed. Applicants appreciate the Examiner's comments with respect to claim 58, and have corrected the listing of claim 58 to accurately reflect the "canceled" status of claim 58. Accordingly, claims 1, 3-11, 13-45, 62-65, 95-101, 106-113, 117, and 123 will be pending in the application upon entry of the claim cancellations and amendments presented herein.

Applicants have amended the claims to more clearly delineate the invention and to correct typographical errors. Support for the amendments can be found throughout the specification and in the claims as originally filed. No new matter has been added.

Amendment and cancellation of the claims herein is not are not be construed as acquiescence to any of the rejections/objections set forth in the instant Office Action and were done solely to expedite prosecution of the application. Applicants hereby reserve the right to pursue the claims as originally filed or similar claims in this or one or more subsequent patent applications. No new matter has been added. Applicants request reconsideration of the subject application based on the following remarks.

Applicant thank the Examiner for the thorough and thoughtful examination of the application and respectfully request reconsideration and withdrawal of the rejections presented in the Office Action.

Claim Rejections – 35 U.S.C. §112

Claims 9, 11-30, and 33 are rejected under 35 U.S.C. §112, first paragraph

Claims 1-9, 11-30, and 33 are rejected, in that the specification allegedly does not reasonably enable any person skilled in the art to make and use the invention commensurate in scope with the claims. In particular, the Office Action sets for the allegation that the

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specification does not enable a method of enhancing any chemical reaction of any molecule.

Applicants. Applicants respectfully disagree and traverse the rejection.

Without acquiescing in any way to the rejection and in order to expedite prosecution of the application, Applicants have amended claim 1 to remove the recitation of "a chemical reaction," and have replaced it with "chemical digestion or chemical alteration." Support can be found at least at page 8, lines 1-10; page 18, lines 35-36; page 20, lines 1-7; and claim 12 as originally filed. Additionally, claim 1 has been amended to recite "biomolecules." Support can be found at least at page 6, lines 15-22; page 18, lines 5-10; and claim 2 as originally filed.

The invention provides a number of advantages over the state of the art at the time the application was filed. Current methods of chemical digestion or chemical alteration of various biomolecules often require extended reaction times, lead to analysis problems, result in side reactions, and are difficult to reproduce (page 2, lines 14-30). In contrast, the amended claims are directed to methods of chemical digestion or chemical alteration of a biomolecule with a surfactant of formula I. Such digestion and alteration reactions are improvements over current methodologies in that they proceed to further completion, reduce the time request for digestion, and eliminate the number of steps required with sample preparation. Such improvements overcome the shortcomings of the current methodologies listed above.

The Applicants' specification is clearly enabled for the scope of the claims by disclosing multiple examples of chemical digestion and alteration of biomolecules. Example 3, Table 2, and Figure 2 clearly show an increase in digestion of various biomolecules in the presence of a surfactant of formula I. Examples 4 and 5 also demonstrate the digestion of various biomolecules in the presence of a surfactant of formula I. Additionally, Example 8 and Figure 5 shows a chemical alteration of a disulfide bond in the presence of a surfactant. Specifically, Figure 5 demonstrates the reduction of a disulfide bond both in the presence and absence of a surfactant. Applicants therefore contend that the specification is fully enabled for the scope of the amended claims and have provided numerous working examples.

Under the Wands factors, the specification fully enables the scope of the claims presented herein, which are directed to the digestion or alteration of a biomolecule using a surfactant. Applicants further submit that the invention teaches an improvement over the known prior art. Specifically, the invention teaches methodologies that proceed further to completion,

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reduce the time request for digestion, and eliminate the number of steps required with sample preparation.

The Office Action alleges that not all proteins of the invention may completely dissolve in the presence of surfactants. Applicants contend that Example 3, Table 2, and Example 4 clearly demonstrate that the digestion of a variety of proteins is improved by the addition of a surfactant. Additionally, Example 3, Table 2, and Example 4 provide sufficient guidance and ample working examples for the methods of digestion or alteration of biomolecules in the presence of a surfactant of formula I. Applicants submit that no undue experimentation is necessary because of the amount of guidance provided in the application, the specific working examples requiring not more than routine procedures to determine biomolecules and surfactants, and the high level of skill in the art at the time the application was filed. Moreover, the Court of Appeals for the Federal Circuit has made it clear that claims are not enabled merely because some experimentation is required and that a considerable amount of experimentation is permitted, as long as such experimentation is not under.

Applicants respectfully submit that the claims presented herein are fully enabled by the application and, therefore, request reconsideration and withdrawal of the enablement rejection.

Claims 17, 20 and 21 are rejected under 35 U.S.C. §112, second paragraph

Claim 17 is rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite, due to the recitation of the terms "S. aureus" and "V8 proteus". Applicants have amended claim 17 to remove the term "S. aureus" and to clarify the term "V8 protease," which is a protease used in the invention for the digestion of molecules. Support can be found at least at page 20, line 35 to page 21, line 8. Applicants submit that the rejection is no longer applicable to claim 17 as amended.

Claims 20 and 21 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Claim 20 is rejected regarding the phrase "favorable chemical property," and claim 21 is rejected as dependent on an indefinite base claim. Applicants traverse and submit that the definition of a "favorable chemical property" is delineated in the specification at page 7 of the application as filed. Applicants indicate that favorable chemical properties include more complete reaction, increased yield, increased rate, and increased utility. Applicants have amended claim 20 to reflect the language of amended claim 1. Additionally, Applicants have

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amended claim 21 to delete the phrase "increased utility." Applicants submit that the rejection is no longer applicable to claims 20 and 21 as amended.

Applicants respectfully submit that the claims 17, 20 and 21 as amended are sufficiently definite within the meaning of the second paragraph of 35 U.S.C. §112 and, therefore, request reconsideration and withdrawal of the indefiniteness rejection.

Claim Rejections – 35 U.S.C. §§ 102 and 103

Claims 1-9, 11, 20-30, and 33 are rejected under 35 U.S.C. §102(b)

Claims 1-9, 11, 20-30, and 33 are rejected under 35 U.S.C. §102(b) as being anticipated by Lee, *et al.* (WO 00/70334). The Office Action sets for the allegation that WO 00/70334 discloses a method of solubilizing a substance comprising contacting the substance with a surfactant of Applicants' formula I, and that "solubilizing" reads on "enhancing a chemical reaction." Applicants respectfully disagree and traverse the rejection.

However, without acquiescing to the rejection and in order to expedite prosecution, Applicants have amended claim 1 to recite "chemical digestion, chemical alteration or a combination thereof." Support can be found at least at page 8, lines 1-10; page 18, lines 35-36; page 20, lines 1-7; and claim 12 as originally filed. Applicants have also amended claim 1 to recite "biomolecules." Support can be found at least at page 6, lines 15-22; page 18, lines 5-10; and claim 2 as originally filed. Applicants submit that claim 1 as amended, and the claims depending therefrom, are novel over WO 00/70334, and respectfully request reconsideration and withdrawal of the anticipation rejection.

Claims 1-9, 11-30, and 33 are rejected under 35 U.S.C. §103(a)

Claims 1-9, 11-30, and 33 are rejected under 35 U.S.C. §103(a) as being unpatentable over Lee, *et al.* (WO 00/70334) in view of Park *et al.* (Anal. Chem. 2001, 73, 2558-2564) and in view of Nelson (US 6,093,541). Applicants respectfully disagree and traverse the rejection.

It is asserted in the Office Action that: (1) Lee teaches a method of solubilizing a substance using a surfactant of the invention; (2) Park teaches protein digestion and (3) Nelson teaches the use of mass spectroscopy in the analysis of certain digestion reactions. It is then

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concluded that the combination of (1), (2), and (3) renders the Applicants' instantly claimed subject matter *prima facie* obvious.

To establish a *prima facie* case of obviousness, three criteria need be met: (i) there must be a suggestion or motivation to modify the reference or combine the teachings; (ii) there must be a reasonable expectation of success; and (iii) the prior art reference must teach or suggest all the claim limitations. See, MPEP 2143. Applicants submit that at least one of the three criteria is not met in the rejection stated in the Action.

Applicants have amended claim 1 to recite "chemical digestion or chemical alteration," and have deleted the phrase "a chemical reaction" (*supra*).

The Examiner admits in the Office Action at page 10 and page 11 that WO 00/70334 does not expressly teach a method wherein a biomolecule is chemically digested or altered in the presence of a protease. Additionally, Applicants acknowledge the Examiner's assertion in the Office Action at page 10 and page 11 that WO 00/70334 does not expressly teach a method further comprising separating the resulting biomolecule fragments.

WO 00/70334 is generally directed toward anionic surfactants, a method of performing electrophoresis, and in one aspect, is directed toward a method of solubilizing a substance using a surfactant. Applicants contend that the teachings of WO 00/70334 are distinct from the instant invention in that the instant invention is directed toward chemical digestion or chemical alteration.

As Applicants understand, Park describes a method of thermal protein denaturation followed by trypsin digestion (see Abstract). The experimental section of Park clearly details the procedures for the digestion steps, which do NOT include, teach or suggest the use of a surfactant. As Applicants understand, Nelson describes a mass spectrometry presentation apparatus, which is able to distinguish modified biomolecules, wherein the modification of biomolecules may include contact with a protease. Nelson also does NOT include, teach or suggest the use of a surfactant.

Neither Park nor Nelson, whether alone or in combination, teaches or suggests any chemical digestion or alteration using a surfactant, and more specifically, neither Park nor Nelson teaches or suggests any chemical digestion or alteration using a surfactant of Applicants' claim 1. At best, Park simply provides exemplification of the digestion of proteins using a protease, and Nelson simply teaches an apparatus, which can analyze such modified compounds.

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Neither disclosure speculates that the addition of a surfactant can be used to enhance any chemical digestion or alteration.

Therefore, the teachings of Park and Nelson, whether alone or in combination, do not provide any motivation that a surfactant can be used to enhance a chemical digestion or alteration. Additionally, any combination of Park and Nelson, combined with the teachings of Lee, does not provide any motivation to use a surfactant to enhance a chemical digestion or alteration, as Lee is directed toward a method of solubilizing a substance.

In contrast to the references cited *supra*, the instant invention clearly demonstrates the unexpected results and advantages of using a surfactant to enhance a chemical digestion or alteration of a biomolecule. Such advantages include more rapid, reproducible, relatively low temperature digestion of a biomolecule, which requires less protease due to enhanced efficiency of the reaction without concomitant increase in miscleavages. Such reactions result in more complete reactions and afford an increased number of correctly cleaved fragments (page 3, lines 5-12). Additional unexpected results and advantages of the instant invention include greater mass spectrometric sensitivity in the presence of the surfactants, even in the presence of degradation products (page 5, lines 26-29).

A *prima facie* case based on the combination of WO 00/70334, Park and Nelson is not established at least for failure to provide motivation to use the WO 00/70334 disclosure to teach the claimed subject matter. Furthermore, the Lee and Nelson teachings does not teach or suggest a specific procedure or method to use a surfactant, and thus cannot necessarily be taken as a teaching of Applicants' subject matter. Based on the foregoing, Applicants submit that the teachings in WO 00/70334, whether alone or in combination with Park and/or Lee, do not teach or suggest Applicants' claimed subject matter. As such, Applicants submit that the rejection should be withdrawn.

Obviousness-type Double Patenting

Claims 1-7, 22, 23, and 25-27 are provisionally rejected in view of Application No. 10/169,002. Applicants submit that this provisional rejection will be addressed upon allowance of the instant claims.

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CONCLUSION

It is believed the application is in condition for immediate allowance, which action is earnestly solicited. Should any of the claims not be found to be allowable, the Examiner is requested to telephone Applicants' undersigned representative at the number below. Applicants thank the Examiner in advance for this courtesy. The Examiner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Dated: September 26, 2007

Respectfully submitted,

By 
Dwight D. Kim, Ph.D.

Registration No.: 57,665

EDWARDS ANGELL PALMER & DODGE LLP

P.O. Box 55874

Boston, Massachusetts 02205

(617) 439-4444

Attorneys/Agents For Applicant